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Anatomy There are 2 kidneys, they are bean shaped and reddish brown

- Located between the peritoneum and the posterior abdominal wall.

- Dimensions: 4 x 2 x 1 inches

- Formed of 2 Layers:

* Cortex: superficial layer containing the nephrons

* Medulla: inner portion, arranged in pyramids, there are 8 – 18 **pyramids** per kidney separated by renal columns. The apex of each pyramid extends towards the renal pelvis and forms a **papilla** which projects into minor calyces then forming major **calyces**, which in turn unite to form **renal pelvis**

- **The nephron:** the functional unite of the kidney

* There are approximately one million nephros in each kidney The number of nephrons is constant from birth

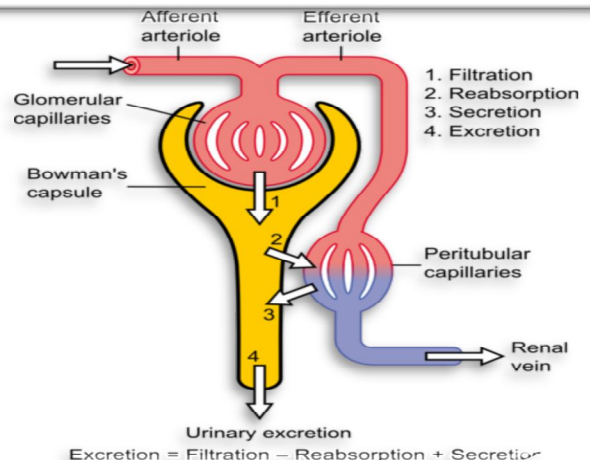
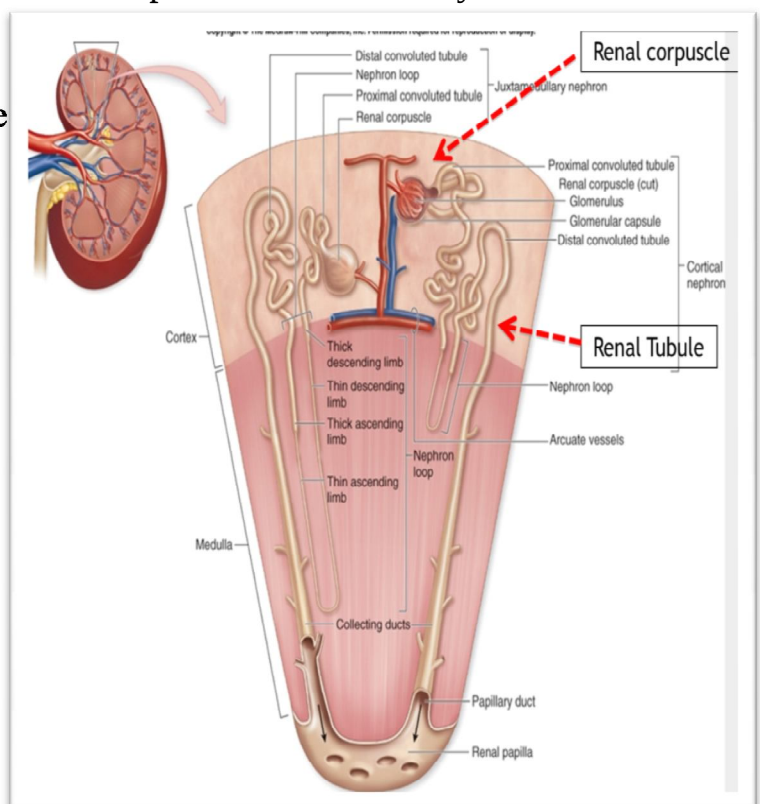
* *It consists of:*

1. Renal corpuscle: Bowman's capsule (glomerulus: site of filtration).
2. Proximal convoluted tubule (PCT)
3. Loop of Henle
4. Distal convoluted tubule (DCT)
5. Collection duct

Renal blood flow:

- 20 – 25 % of cardiac output

- Renal artery divides to inter-lobar arteries (run between the medullary pyramids) **then** arcuate arteries (run in the corticomedullary junction) **then** interlobular arterioles (run in the cortex) **then** afferent arterioles of Glomeruli **then** efferent arterioles which divide into the vasa recta and the peritubular capillaries, this is a network of capillaries which allows movement of fluids and solutes out of the tubules



Functions:

- * Regulation of water & electrolyte balance
- * Regulation of acid base balance
- * Excretion of water soluble waste: urea, uric acid, creatinine, drugs
- * Endocrine:

1- Secretion of hormones :

- Renin & prostaglandins : for regulation of BP.
- Erythropoietin : for production of red cells in bone marrow.

2- Degradation of peptide hormones e.g. insulin.**3- Activation** of vitamin D**A) Glomerular Function****Features of the glomerular filtrate:-**

<u>Volume (GFR)</u>	100-130 ml/min (180 L/d).
<u>Composition</u>	similar to plasma without its macromolecules proteins & lipids
<u>Specific gravity</u>	1010 (isotonic to plasma)

Factors affecting the glomerular filtrate:-

- 1- Permeability of the glomerular barrier:
2. Forces across the glomerular barrier :
 - Glomerular capillary hydrostatic pressure.
 - Bowman's space hydrostatic pressure.
 - Plasma osmotic pressure.
3. Surface area of the glomerular barrier.
4. Molecular weight & electrical charges of plasma molecules.

Glomerular filtration rate (GFR):-

- It is the volume of fluid filtered from the renal glomerular capillaries into Bowman's capsule per minute
- In man: GFR = 125 ml/min
- In women: 10 % less than those of men
- Although the GFR is about 180 L/day, our urine output is only 1 -2 L/day (which is good or else we'd spend the day in the bathroom)

$$GFR = \frac{\text{Urine Concentration} \times \text{Urine Flow}}{\text{Plasma Concentration}}$$

stages of chronic kidney diseases:-

Stage	GFR
1	≥ 90
2	60 – 89
3	30 – 59
4	15 – 29
5	< 15

B) Tubular function**I- Proximal Tubule:****A- Reabsorption** Na pump (Na-K/ATPase).

- complete reabsorption of:-
glucose - amino acids - K - HCO₃.
- About 60-70 % of Na, Cl, Ca & P.
- passive reabsorption of about 60-70 % of H₂O depending Na.

B- Secretion

- * hydrogen ions.
- * uric acid.
- * creatinine.
- * drugs e.g. penicillin.

II- Loop of Henle : "Counter-current multiplier system"

- Active reabsorption of 25 % of Cl & Na (thick ascending limb).

- Passive reabsorption of 15 % of H₂O (descending limb dependig on hypertonicity of medullary interstitium).

III- Distal & Collecting Tubules :

A- Reabsorption	B- Secretion
- About 10-20 % of Na, Cl, Ca, P & HCO₃. - passive reabsorption of variable % of H₂O responsible for regulation of volume & specific gravity of urine.	* hydrogen ions. * K. * NH₃. * drugs e.g. salicylates.

N.B. a Functions of distal & collecting tubules are under control of hormones ~

- Aldosterone stimulates reabsorption of Na & secretion of K & H.
- ADH stimulates reabsorption of H₂O.
- PTH stimulates reabsorption of Ca & inhibits reabsorption of P.

Role of kidney in sodium balance:

Glomerulus	PCT	loop of Henle	DCT
Free filtration	Reabsorption		
	60-70 %	25 %	10-20 % by aldosterone

Role of kidney in H₂O excretion:

Glomerulus	PCT	loop of Henle	DCT & collecting tubules
Free filtration (180 L/d)	Reabsorption		
	60-70 % Depending of Na	15 % depending on Medullary hypertonicity	10-20 % under control of ADH

ADH : (regulation of volume & specific gravity of urine)

- Increased osmotic pressure of blood → stimulation of osmoreceptors of hypothalamus → secretion of ADH → increased permeability of collecting ducts ~ increased reabsorption of H₂O by hypertonic interstitial fluid → decreased volume & increased specific gravity of urine.*
- Decreased osmotic pressure of blood ~ decreased ADH → decreased permeability of*

Role of kidney in acid-base balance:

- Reabsorption of HCO₃ mainly in the PCT.
- Generation of new HCO₃ mainly in the DCT through excretion of NH₃.
- Both processes are dependant on active secretion of H⁺ ions.

Role of kidney in excretion of metabolic waste products:

- Glomerular-filtration of e.g. urea, creatinine & uric acid.
- Tubular secretion of:
 - organic acids e.g. uric acid.
 - organic bases e.g. creatinine.
 - drugs e.g. penicillin.

Investigations of Renal Diseases

1) Urine investigations :

- 1- Urine analysis. (see table page 5)
- 2- Urine culture & sensitivity (for urinary tract infections)

2) Blood investigations :

- 1- CBC.
- 2- Urea, creatinine & uric acid levels.
- 3- Electrolytes & ABG : Na, K, Ca, P, pH, HCO₃.

Na:	135 – 145 mEq/L
K:	3.5 – 5 mEq/L
Ca:	8.5 – 10.5 mg%
P:	2.5 – 4.5 mg%
HCO ₃ :	22 – 26 mEq/L

3) Renal function tests :-

A. Glomerular Functions :

1- Measurement of :

Serum creatinine (N : 0.7 – 1.4):

- Produced from **muscles** at a constant rate
- So its plasma concentration depends on its excretion, which reflects **GFR**
- **Small** change in creatinine are associated with **large** change in GFR
- So plasma creatinine is an **insensitive marker of early renal disease**

Blood urea (N: 20 – 40 mg %):

- Less reliable as it is affected by dietary protein & liver failure

2- Clearance tests :

1- Creatinine clearance : (C_{cr})

Def:- Volume of plasma which is cleared from creatinine in one minute

- It is the most widely used test.
- It is calculated from the following formula

$$\text{creatinine clearance} = \frac{\text{Ucr (urine cr)} \times V \text{ (volume of urine ml/d)}}{\text{Pcr (plasma creatinine)} \times 24 \times 60}$$

Or roughly by

$$\text{- Cockcroft-Gault equation} = \frac{(140 - \text{age}) \times (\text{Wt in kg})}{(72 \times \text{Cr})} \times (0.85 \text{ if female})$$

- It is normally 100 - 130 ml/min.
- It is a good estimate of GFR.

2. Others:- Inulin clearance - Cr51- EDTA clearance - Urea clearance (not accurate).

B. Tubular Functions :

- 1- Specific gravity & osmolality of urine
- 2- Urine concentration test.
- 3- Urine acidification test.
- 4- Fractional excretion of Na (FENa).

4) Renal imaging :

a- Plain X-ray of urinary tract (KUB).

b- Renal ultrasound: it demonstrates

Size:- Bipolar renal length (8.5 – 13.5 cm):- In **CRF**: the kidneys are small **except** in:-

- Polycystic kidney disease: large with multiple cysts

- Diabetic nephropathy

- Amyloidosis: normal size

- In **ARF**: the kidneys are normal size or may be swollen**Doppler** ultrasound is useful to assess renal blood flowRenal **stones**, **mass** lesions, **cysts**

c- IVP & ascending pyelography.

d- CT & MRI.

e- Radionuclide studies.

f- Renal arteriography.

5) Renal biopsy.**6) Investigations for detection of the cause****Normal Urine Analysis**

Physical	Chemical	Microscopic
1. Volume : 0.8-1.5 L/d	5. Proteins : < 150 mg/24 hours	a. <u>Cells</u> :-
2. Aspect : amber yellow, clear	6. Pigments : urobilinogen	- RBCs : 0-2/hpf
3. Specific gravity : 1015-1025	7. Glucose : Nil	- WBCs : 0-5/hpf
4. pH : 5-7	8. Ketones : Nil	- Epithelial cells : few
		- Bacteria, parasites, ova, malignant cells: absent
		b. <u>Casts</u> : few hyaline
		c. <u>Crystals</u> : few oxalate

Casturia:- increased casts in urine1- **Excess hyaline casts** :

- Concentrated urine.

- All causes of proteinuria especially nephrotic syndrome.

2- **Lipid casts** : nephrotic syndrome.3- **Granular casts** : severe advanced renal disease (renal failure).4- **Broad casts** : advanced renal failure.5- **Red cell casts** : glomerulonephritis, vasculitis.6- **White cell casts** : pyelonephritis, interstitial nephritis.7- **Epithelial casts** : acute tubular necrosis, interstitial nephritis, glomerulonephritis.

Glomerular Diseases

- 1- Immune : Glomerulonephritis.
- 2- Metabolic : Diabetes mellitus - Amyloidosis.
- 3- Hereditary : e.g. Alport's syndrome.

Glomerulonephritis

Definition: Group of disorders characterized by bilateral, symmetrical glomerular injury of immunological origin that affects both kidneys

Mechanism & aetiology:-

I- Immune complexes deposition: 3 mechanisms

Accordingly this type of injury may occur with:

Mechanism	Aetiology		
A. Exogenous antigens	Drugs		Infections
	e.g. Penicillin - D-penicillamine		- <u>Bacteria</u> e.g. streptococci, staphy
			- <u>Viral</u> : HBV, CMV, EBV
			- <u>Parasite</u> : Shistosoma, Plasmodium
B. Endogenous antigens	Host DNA	Tumor antigens	RBCs membrane
	In SLE	- Gastrointestinal carcinoma. - Lymphoma.	
C. Failure to clear immune complexes		SLE	

II Antiglomerular basement membrane antibody (anti-GBM):

This is IgG that reacts with antigen on glomerular and alveolar capillary basement membrane leading to **Glomerulonephritis + hemoptysis** (Good pasture's syndrome).

III T-cell dysfunction: May play role in minimal lesion nephropathy or focal glomerulosclerosis.

Pathology: Pathology is determined by renal biopsy examined by:

1. Light microscopy
2. Electron microscopy
3. Immunofluorescence

	Pathological changes	CIP
Minimal	Light microscopy: -Free ± lipid droplets Electron microscopy: - Fusion of the foot processes	Nephrotic syndrome
Focal segmental	Focal (some glomeruli) - segmental (some parts of this glomeruli) sclerosis & hyalinosis	
Membranous	1- Diffuse thickening of capillary wall	
Membrano-proliferative	1- as above + 2- Proliferation of mesangial cells & matrix = splitting or reduplication of GBM (tram-like appearance)	Mixed
Mesangio-proliferative	1-2 as above + 3- Mesangial deposits of immunoglobulins . Special type (Berger disease: - IgA nephropathy).	Mixed Or haematuria
6. Diffuse proliferative	Proliferation of: - (hypercellular + bloodless) 1- endothelial cells: - narrowing or occlusion of capillaries. 2- epithelial cells: - formation of crescents in severe cases. 3- Infiltration by inflammatory cells (neutrophils & monocytes).	Nephritic
7. Crescentic	excessive proliferation forming epithelial crescents in majority of glomeruli	Rapidly progressive (ARF)
8. Chronic	- gradual glomerular & tubular atrophy and interstitial fibrosis. - It is the end-stage of other types of GN especially the severe ones.	CRF

Membrano proliferative GN: - Caused by exogenous antigens (HBV, HCV) or endogenous antigens (malignancy, SLE).

Mesangioproliferative glomerulonephritis: Caused by: IgA nephropathy, SLE, Bilharziasis.

- o Due to deposition of IgA + C3 in glomerulus.
- o Usually follows upper respiratory tract infection.
- o Most common glomerulopathy world wide.
- o Common in young adult.
- o 20% develop nephrotic syndrome.
- o Renal insufficiency may occur in 20% of cases after 20 years

There's poor correlation between pathology and clinical presentation, however:

- 1- Cases presenting by nephritic syndrome are usually: Diffuse proliferative or membranoproliferative GN
- 2- Cases presenting as nephrotic syndrome are usually: Minimal change, membranous or membranoproliferative glomerulonephritis.

Clinical presentation:

Glomerulonephrits may present as:

- 1- Asymptomatic hematuria or proteinuria.
- 2- Nephritic syndrome.
- 3- Nephrotic syndrome.
- 4- Acute renal failure.
- 5- Chronic renal failure.



NEPHRITIC SYNDROME

Definition: Diseases characterized by acute onset of
 1- Oliguria -\+ haematuria 2- Hypertension. 3- Oedema.

Aetiology:-

I. 1ry GN: Proliferative - membrano-proliferative GN - good-pasture syndrome

II. 2ry GN: (4 Is)

1- Infections:

Bacterial: Group-A hemolytic streptococci (most common) particularly strains 3, 4, 12 in cute tonsillitis & type 49, 2, 51 in pyoderma.

Viral: HBV, CMV, EBV.

Parasitic: Shistosoma, plasmodium.

2- Iatrogenic: e.g. Penicillin.

3- Immunological diseases: e.g. SLE, Rheumatoid, PAN.

4- Others:- Irradiation - Kidney rejection.

ACUTE POST-STREPTOCOCCAL GLOMERULONEPHRITIS (PSGN)

- **Nephretogenic** strains of group A, B-haemolytic streptococci (types 4, 12 & 49).
- Site of infection:- pharyngitis or skin (pyoderma or impetigo).
- Latent period of 1-3 weeks.
- Age:- below 20 years (mean age : 7 years).
- Sex:- Males > females (2:1).

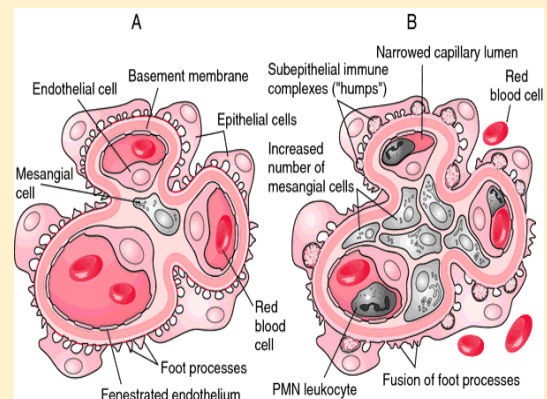
Pathogenesis: deposition of immune complexes with complement in the glomeruli.

Pathology: "Features of diffuse proliferative GN"

Light microscopy : see table page 7

Immunofluorescent microscopy: Granular deposits of IgG & C₃ .

Electron microscopy: Subepithelial "humps"



Pathological change	C/P
Injury of glomeruli	Haematuria
- Decreased GFR - Salt & water retention - R-A system	Oliguria Oedema HTN
Severe injury - Tube obstruction - ATN	Impairment of KFTs

Clinical Picture :

The disease presents with acute nephritic syndrome i.e. acute onset of haematuria, oliguria, usually with oedema & hypertension.

1. Haematuria :

- Usually in the form of dark or smoky urine but frank haematuria may occur
- Pathogenesis : injury of the capillary wall.

2. Oliguria : due to decreased glomerular permeability (**Low GFR**).

3. Nephritic oedema :

- Of acute onset.
- Appearing in periorbital region & face, then may involve perigenital area, sacrum, lower limbs & hands.
- Rarely it becomes generalized.
- Pathogenesis : salt & water retention due to decreased glomerular permeability.

4. Cardiovascular manifestations :

A) Hypertension :

- It is due to salt & water retention.
- Severe hypertension may lead to HF , pulmonary oedema, encephalopathy, papilloedema & retinal hemorrhage.

B) Circulatory congestion:

- Congested pulsating neck veins & pulmonary congestion
- Due to hypervolaemia or uncommonly heart failure.

5. General manifestations :

- Fever, headache & malaise.
- Anorexia, nausea & vomiting.
- Pain in both loins.
- Pallor due to oedema & anaemia.

6. Temporary impairment of renal functions :

- May occasionally end in acute renal failure in severe cases.
- Pathogenesis : - injury of glomeruli.
 - thrombosis of glomerular capillaries.
 - acute tubular necrosis due to glomerular ischaemia.
 - tubular obstruction by casts.

Investigations:**1. Urine analysis :**

- Volume : oliguria.
- Aspect : **dark or smoky** urine but frank haematuria may occur.
- Specific gravity : **increased**.
- Proteins:- **less than 3.5 gm/24 hours** & non-selective.
- Microscopic examination :
 - Cells : excessive **RBCs** & **WBCs**.
 - Casts : **red cell**, white cell, epithelial & hyaline casts.

N.B. The presence of RBCs & red cell casts is the most important finding.

2. Blood investigations :

- Anaemia
- High ESR.
- Serum K may be elevated.
- Normal plasma proteins & lipids.

3. Renal function tests :

- Blood urea & serum creatinine may be elevated.
- Decreased creatinine clearance (a good estimate of GFR).

4. Renal imaging : Abdominal ultrasonography may show mild swelling of kidneys.**5. Renal biopsy :** Usually not needed for diagnosis & indicated only in prolonged cases to exclude other diseases.**6. Investigations for the cause :**

- High ASO titer & positive streptozyme test.
- Decreased serum complement (C3).
- Culture : swabs from throat & inflamed skin

Prognosis:

- *It is a self-limited disease in most patients. - Prognosis is better in children.*
- *Over 90 % of patients : complete recovery usually in few weeks.*
- *About 5 % of patients : development of rapidly progressive glomerulonephritis which leads to renal failure within weeks to months.*
- *Few patients: death occurs on top of acute renal failure, acute pulmonary oedema or hypertensive encephalopathy.*

Differential Diagnosis:

1. Other causes of nephritic syndrome (See before)
2. Nephrotic syndrome.
3. Other causes of oedema.
4. Other causes of haematuria.

Treatment

1. Complete rest in bed.

2. Diet:

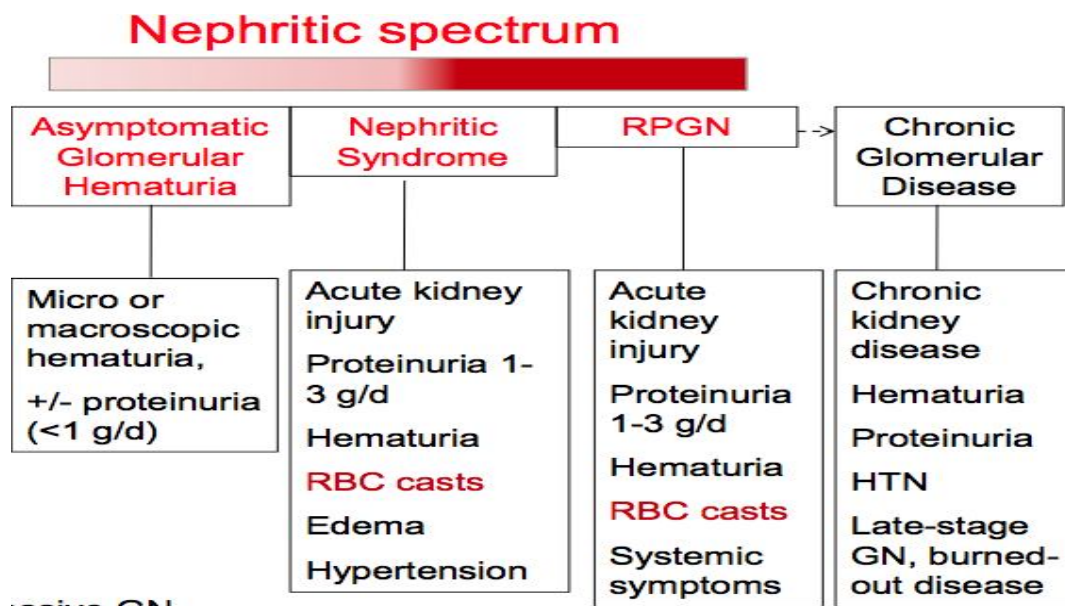
- Salt restriction.
- Fluid restriction is indicated if oliguria & oedema are marked.
- Protein restriction only in cases of renal failure.
- Potassium restriction in cases of hyperkalaemia.
- Carbohydrates are given freely.
- Fats are usually not preferred by the patient being nauseating.

3. Antibiotics : e.g. crystalline penicillin 1 million IU/6 hour IV for 1 week for eradication of streptococcal infection.

4- Symptomatic treatment :

- For hypertension & oedema :
 - salt & fluid restriction.
 - diuretics e.g. frusemide.
 - antihypertensive drugs e.g. hydralazine.
- For hyperkalaemia : (See later).

5. Treatment of complications: e.g. acute renal failure, acute pulmonary oedema & hypertensive encephalopathy.



NEPHROTIC SYNDROME

Definition:- It is a clinical syndrome characterized by :

- 1- Heavy proteinuria (more than 3.5 gm/24 hours in adults).
 - 2- Hypoproteinaemia.
 - 3- Generalized oedema.
 - 4 - Hyperlipidaemia.
- *The primary abnormality in nephrotic syndrome is the heavy proteinuria with other manifestations occurring secondary to it.*

Aetiology:

1. Primary glomerulonephritis:

- Minimal lesion GN (the most common cause in children)
- Membranous GN (the most common cause in adults).
- Membranoproliferative GN.
- Focal segmental glomerulosclerosis.

2. Secondary (3Is + 3Ms)

- A- Immune diseases :** - SLE, PAN & anaphylactoid purpura - Serum sickness.- Mixed cryoglobulinaemia.
- B. Infections :-** Hepatitis C & B. - HIV nephropathy. - Infective endocarditis. - Syphilis. - Malaria. - Schistosoma mansoni.
- C. Iatrogenic:-** Drugs : captopril, penicillamine. - Heroin. - Heavy metals (gold, mercury).
- D. Metabolic diseases :** - Diabetic nephropathy. - Renal amyloidosis.
- E. Malignant diseases :** e.g. Hodgkin's disease & solid tumours.
- F. Mechanical :-** Renal veins thrombosis. - IVC obstruction - severe right-sided heart failure - constrictive pericarditis - pericardial effusion.
- Hypertensive nephrosclerosis (rare).

***Congenital (Alport syndrome):** nephrotic syndrome + nerve deafness*

Pathogenesis:

- 1. Heavy proteinuria:** - Increased glomerular permeability (damage of GBM + reduction of -ve charge).

a) Selective proteinuria	b) Non-selective proteinuria
low molecular weight (e.g. albumin) - mild with good prognosis	low & high molecular weights - marked with bad prognosis

2. Hypoproteinaemia:

- It is due to loss of proteins in urine and decreased intake & absorption of proteins.

3. Generalized oedema : due to

- Hypoalbuminaemia (the most important factor)
- Salt & water retention:- due to secondary ***hyperaldosteronism*** & increased ***ADH***.

4. Hyperlipidaemia : (Increased cholesterol & triglycerides)

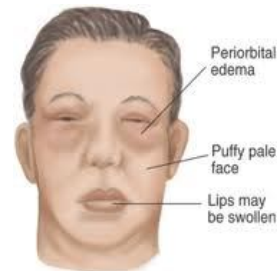
- It may be due to : - increased hepatic synthesis of lipids.
- decreased lipid catabolism (Loss of lipase enzyme)

5. Others:-

Hypokalaemia	Hypocalcaemia
-Secondary hyperaldosteronism. - Decreased intake due to anorexia. - Decreased absorption due to oedema of intestine. - Effect of drugs e.g. diuretics, corticosteroids.	- I decrease of protein-bound Ca (hypoalbuminaemia). - It rarely results in tetany as ionizable Ca is normal.

Clinical Picture :**1. Nephrotic oedema :**

- It is of **gradual** onset & may show remissions & exacerbations.
- It begins in the **periorbital** region, **face** then involves perigenital area, sacrum, lower limbs & hands. (**morning: face oedema - night: ankle oedema**)
- It may become **generalized** and associated with ascites and pleural & pericardial effusions (generalized anasarca).
- The oedema is soft & **pitting**.
- may lead to hypotension (reduced B. volume)

**HTN in Nephrotic S**

- feature of the **cause** (SLE)
- complications of **atherosclerosis**
- **Renal failure**

2. Pallor : due to oedema & anaemia.**3. Gastrointestinal manifestations :** anorexia, nausea, vomiting & diarrhoea due to oedema of gastric & intestinal mucosa.**4. Parotid enlargement, white nails (leuconychia), myodema, muscle wasting & osteoporosis :** may be present due to hypoproteinaemia.**5. Features of the cause :** e.g. DM, SLE.**6. Features of complications :-**

Decreased	C/P
Gammaglobulins & Complement	Increased incidence of infections especially of lungs, skin & peritoneum
Transferrin	Anaemia
Antithrombin-III +: <i>increased liver synthesis of fibrinogen + hyperlipidemia</i>	Thromboembolism
vitamin D-binding globulin	Osteomalacia Osteoporosis (hypoproteinaemia)
Thyroxin binding globulin	decreased thyroxin level
Hypokalaemia & hypocalcaemia:- see later	

- **Atherosclerosis** due to hyperlipidaemia.
- **Hypotension** & shock.
- **Malabsorption** due to intestinal oedema.
- Attacks of abdominal pain (**nephrotic crisis**).
- PCT dysfunction: leading to **glycosuria, aminoaciduria & Fanconi S.**
- **Renal failure & hypertension:-**
 - CRF may occur due to progression of underlying disease.
 - ARF may occur due to: - hypovolaemia leading to pre-renal failure.
 - bilateral renal vein thrombosis ??.

Investigations:

1. Urine analysis :

- Volume : normal.
- Aspect : frothy.
- Specific gravity: **increased**.
- Proteins : - **heavy proteinuria** : more than 3.5 gm/24 hours.
 - may be selective or non-selective (urine electrophoresis).
- Microscopic examination:
 - Casts: fatty casts (**characteristic**) & hyaline casts.
 - **Lipiduria** : in form of fatty casts & oval fat bodies.

Good prognosis expected with:-

- minimal change GN - children - selective proteinuria

Bad prognosis is expected in:

- Proliferative or crescentic GN
- Non-selective proteinuria.
- Glomerulosclerosis.

Blood investigations :

- Plasma proteins : **hypoproteinaemia** mainly hypoalbuminaemia.
- Plasma lipids : **increased** cholesterol & triglycerides.
- Electrolytes : may be decreased **K** & total **Ca**.
- **Anaemia** may be present.

3. Renal function tests : Normal except if renal failure occurs.

4. Renal biopsy:- It is not indicated in all patients e.g. in children since the diagnosis is usually a minimal change (**steroids first without biopsy**).

5. Investigations for the cause : e.g. blood glucose, ANA

6. Investigations for complications.

Differential Diagnosis :

- A) Nephrotic syndrome should be differentiated from :
1. Other causes of oedema e.g. nephritic syndrome
 2. Other causes of proteinuria.
 3. Myxoedema.
- B) Differential diagnosis of the cause.

Treatment

1) Treatment of Hypoproteinaemia :

1. High protein diet (of doubtful value) should be restricted if RF developed.
2. IV salt-free albumin.

2) Treatment of oedema :

1. Bed rest.
2. Salt restriction.
3. Medicinal salts & cation exchange resins may be used.
4. Diuretics :
 - Potassium-sparing diuretics e.g. spironolactone 100 mg/d.
 - Thiazides e.g. dihydrochlorothiazide 25 mg/d.
 - Loop diuretics e.g. frusemide 40 mg/d in resistant cases.
 - Potassium supplementation should be given with thiazides & loop diuretics.
5. salt free albumin

3) Treatment of the cause:- e.g. in minimal lesion GN (more than 60 % of nephrotic syndrome in children & about 20 % in adults) :

1- Prednisone :

- **Dose** : 2 mg/kg/d orally for 4 weeks followed by
1 mg/kg/d orally for 4 weeks followed by tapering over 4 weeks

- Response in children :

- 10 % of cases : show no response (steroid-resistant cases) need renal biopsy.
- 90 % of cases : show initial response & then after withdrawal of steroids :
 - 50 % : permanent remission (steroid-responsive)
 - 50 % : frequent relapses and may become steroid-dependent.

2- Immunosuppressive drugs: Indicated in steroid-resistant & steroid-dependent cases. - Cyclophosphamide 2-3 mg/kg/d for 8 weeks

4) Others (doubtful)

C. ACEI (captopril): Lowers intraglomerular pressure.

D. NSAID: Alter the GBM permeability

4) Treatment of complications:

e.g. infections, anaemia, hyperlipidaemia, thromboembolism.

Nephrotic Syndrome Recap

• Adults main causes

- Diabetes, SLE, amyloidosis, etc. (40%)
- Membranous glomerulonephritis (20%)
- All forms of proliferative glomerulonephritis (15%)
- Minimal change glomerulonephritis (10%)
- Focal glomerulosclerosis (10%)
- Membranoproliferative glomerulonephritis (5%)

• Children main causes

- Minimal change glomerulonephritis (60%)
- Focal glomerulosclerosis (10%)
- All forms of proliferative glomerulonephritis (10%)
- Membranoproliferative glomerulonephritis (10%)
- Membranous glomerulonephritis (5%)
- Secondary to systemic disorder (5%)

ACUTE RENAL FAILURE

(**ARF**) = **ACUTE RENAL INJURY**

Definition :

A condition characterized by **rapid** reduction of renal functions which is frequently **reversible** and usually associated with **oliguria** (less than 400 ml/day).

Aetiology:

A- Pre-renal : (55% "renal Hypo-perfusion")

I- Decreased blood volume (absolute)	II- Decreased renal blood flow (relative)
1. Total loss:- Severe haemorrhage. 2. GIT fluid loss:- Severe vomiting or diarrhoea. 3. Skin fluid loss:- Excessive sweating or Extensive burns. 4. Renal fluid loss:- polyuria or Diuretics.	1. Shock :- Septicaemia or Anaphylaxis. 2. Reduction of cardiac output e.g. severe heart failure . 3. Liver failure (hepatorenal S). 4. Bilateral renal artery occlusion:- Thrombosis - Embolism - Dissection.

B- Intrinsic Renal 40% (diseases of renal parenchyma)

I- Tubular	II- Glomerular	III- Vascular
1-Acute tubular necrosis (ATN) 2- Acute interstitial nephritis. 3- Severe acute pyelonephritis 4-Tubular obstruction: A- Crystals e.g. uric acid. B- Proteins:- - <i>Hb</i> = haemolytic crisis. - <i>Myoglobin</i> = rhabdomyolysis. - <i>Ig</i> = multiple myeloma	1.Membrano-proliferative GN 2.Mesangio-proliferative GN 3.Diffuse proliferative GN= acute GN 4.Crescentic GN=RPGN e.g. Goodpasture's syndrome 5.Renal transplant rejection	1- Malignant HTN. 2- Eclampsia. 3- Vasculitis. 4- DIC. 5- Haemolytic uraemic syndrome 6- Bilateral renal vein occlusion

Acute tubular necrosis (ATN) : (most common cause)

a. Ischaemic : persistent reduction of renal blood flow in cases of prerenal failure.

b. Nephrotoxic:

Exogenous - Antibiotics (aminoglycosides, amphotericin B, cephaloridine) - Cyclosporin - Contrast media - Heavy metals - Solvents - Insecticides.

Endogenous: hyperuricemia, hemolysis

C- Postrenal : 5% (due to obstruction of urine flow)

1. Bilateral ureteric obstruction e.g. calculi, clots, crystals, ligation during surgery.
2. Unilateral ureteric obstruction in patients with solitary functioning kidney.
3. Bladder neck & urethral obstruction (the condition starts with retention of urine)

Pathogenesis of Acute Tubular Necrosis:

The condition of ATN usually passes through four phases:

Initiation phase	kidneys are subjected to the effect of ischaemia or nephrotoxin
Maintenance phase Oliguric phase	There is reduction of GFR & oliguria due to : - Intra-renal vasoconstriction. - decreased glomerular filtration pressure - tubular obstruction. - tubular back-leak of filtrate.
Diuretic phase	Urine output increases up to many liters Structural recovery before functional recovery of the tubules:- patent tubules with delayed recovery of tubular reabsorption function.
Recovery. phase	Regeneration or renal parenchyma & recovery of renal functions occur if the underlying cause is properly corrected

Pathology of Acute Tubular Necrosis:

	Ischaemic	Toxic
Necrosis	Patchy in whole tubule	Diffuse in PCT
Basement membrane	Damaged	Intact

Clinical Picture :

Initial:- C/P of the cause: e.g.

- Shock.
- Recent major surgery.
- Recent exposure to a nephrotoxin.

Maintenance phase**1. Oliguria :**

- Less than 400 ml of urine\ day.
- Absolute anuria is more common in postrenal obstruction.
- Oliguria usually lasts 1-2 weeks but may range between few days & weeks.

2. Hypervolaemia :

- Circulatory congestion: congested neck veins & pulmonary congestion (which may lead to pulmonary oedema).
- Hypertension.
- Oedema & weight gain.
- Drowsiness, convulsions & coma.

3. Hyperkalaemia : (See later).**4. Acidosis :**

Kussmaul's breathing (rapid deep respiration).

Initiation phase	C/P of the cause
Maintenance phase Oliguric phase	1. Oliguria : 2. Hypervolaemia : 3. Hyperkalaemia 4. Acidosis : 5. Uraemic syndrome :
Diuretic phase	- Polyurea - Hypotension, dehydration & electrolyte losses
Recovery. phase	- Return to normal

5. Uraemic syndrome :

- Anorexia, nausea, vomiting, hiccough.
- Anaemia.
- Asterixis (flapping tremors).
- Bleeding tendency, gastrointestinal haemorrhage
- Pruritus.
- Pericarditis, pleurisy.
- Convulsions, twitches, irritability.
- Confusion, coma.

Diuretic phase :

- This phase may occur in some patients before complete recovery.
- The urine volume reaches up to 5-10 L/day.
- This may result in hypotension, dehydration & electrolyte losses (Na & K).

Recovery phase :

If the underlying cause is corrected the GFR rises, urine output returns to normal & clinical manifestations improve.

Investigations :**1. Urine analysis:-**

- Volume : - **less than 400** ml/d.
- absolute anuria is more common in postrenal obstruction.
- Aspect: dark.
- Specific Gravity : **low fixed** " in the range of 1010 " in cases of ATN.
- Proteins : usually mild increase.
- Microscopic examination :
 - Cells : epithelial cells, red cells.
 - Casts : granular, epithelial, red & hyaline casts.

2. Blood investigations :

- Normochromic normocytic anaemia.
- Increased K & P.
- Decreased Na, Ca, HCO₃, pH.

3. Renal function tests :

There is marked impairment of renal functions :

- Increased blood urea, serum creatinine & uric acid levels.
- Decreased creatinine clearance.(a good estimate of GFR).
- Low fixed specific gravity" in the range of 1010 "in cases of ATN.
- Fractional excretion of Na : usually < 1 in prerenal failure & usually > 1 in ATN.

4. Renal imaging :

- Plain X-ray of urinary tract & ultrasonography are mainly required for detection of postrenal obstruction.
- Ascending pyelography, CT & MRI may be also indicated.

5. Renal biopsy: Indicated in cases of: - unexplained ARF.

- persistent ARF > 4 weeks.

6. Investigations for the cause.**7. ECG :** Shows features of hyperkalaemia (See later).**Prevention:** Early detection & proper correction of conditions that may result in ARF:

- In cases of blood, plasma or fluid loss: replacement should be done rapidly to prevent renal ischaemia.
- Nephrotoxic drugs should be used cautiously especially in patients with renal disease.

Treatment**A- First:- for post renal**

Exclusion of urinary retention : by bladder catheterization.

Management of post-renal obstruction:

- By plain X-ray - US - CT - Cystoscopy & ureteric catheterization.
- The presence of obstruction requires urologic consultation and interference.

B- Then:- for renal**1) Treatment of the cause :** e.g.

- IV & oral fluid in hypovolaemia.
- Blood transfusion in haemorrhage & haemolysis.
- Discontinuation of nephrotoxic agents.

Initiation phase	- ttt of the cause - induction therapy
Maintenance phase	- Conservative - Dialysis
Diuretic phase	Replacement therapy

2) Induction of diuresis :

- This could be done using :
 - Frusemide : 2-10 mg/kg IV.
 - Dopamine : 1-3 μ g/kg/min by IV infusion.
 - Mannitol : 500 ml of 25 % solution by IV infusion.
- This may convert oliguric renal failure to non-oliguric type & may prevent development of the maintenance phase of ATN if given early (controversial).

3) Conservative treatment:**a. Diet :**

- Fluid & salt restriction for correction of hypervolaemia.
- Potassium restriction for correction of hyperkalaemia.
- Proteins restriction (0.5-1 gm/kg/day) to avoid rise in level of urea
- Carbohydrates:- Adequate amounts to give calories & limit protein catabolism.

b. Treatment of hypervolaemia :

- Fluid & salt restriction.
- Monitoring of BP, CVP, body weight, urine output & oedema

c. Treatment of hyperkalaemia : (See later).**d. Treatment of acidosis:**

NaHCO₃ by IV infusion is indicated in severe cases e.g. pH less than 7.2

e. Symptomatic treatment : e.g. For

- Hypertension. - Heart failure. - Anaemia. - Nausea, vomiting.
- Correction of hyperphosphataemia :
 - restriction of phosphate in diet.
 - calcium carbonate or aluminum hydroxide gel

4) Dialysis:- - Indications

Laboratory	Clinical
1. Creatinine > 10 mg/dl.	1. Coma, convulsions.
2. Bicarbonate < 10 mEq/L.	2. Pulmonary oedema.
3. K > 7 mEq/L.	3. Pericarditis.
4. Blood urea above 200 mg/dl.	4. Severe bleeding.

- **Methods of dialysis :** 1. Haemodialysis.
2. Peritoneal dialysis.

5) Treatment during the diuretic phase :

1. Adequate fluid intake to avoid hypovolaemia & dehydration.
2. Adequate replacement of electrolyte losses especially Na & K.

Summary of ARF

Phases	CVP	TTT
Initiation:- <i>exposure</i>	CVP of the cause	- ttt of the cause - induction therapy
Maintenance (Oliguric) - <i>Intra-renal VC</i> - <i>decreased GF pressure</i> - <i>tubular obstruction.</i> - <i>tubular back-leak.</i>	1. Oliguria : 2. Hypervolaemia : 3. Hyperkalaemia 4. Acidosis : 5. Uraemic syndrome :	I- Conservative:- a. Diet b. ttt of hypervolaemia c. ttt of hyperkalaemia d. ttt of acidosis e. Symptomatic ttt II- Dialysis
Diuretic:- <i>Structural recovery before function resetting</i>	- Polyurea - Hypotension, dehydration & electrolyte losses	Replacement therapy
Recovery	- Return to normal	

CHRONIC RENAL FAILURE (CRF)

Chronic Renal Injury

Definition : A condition characterized by **progressive & irreversible** reduction of renal functions. The clinical symptoms & signs of **end-stage renal failure** are known as uraemia or uraemic syndrome.

Aetiology: (the most common 2 causes are: DM & CP)

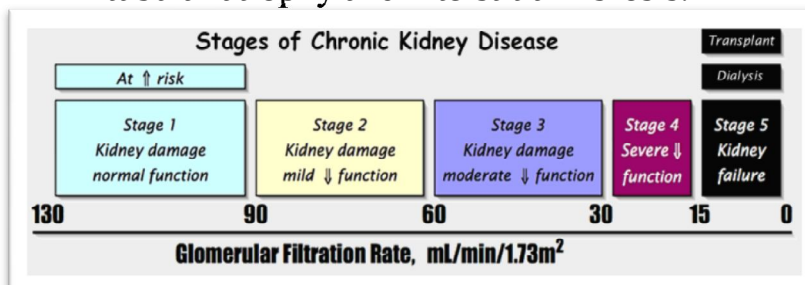
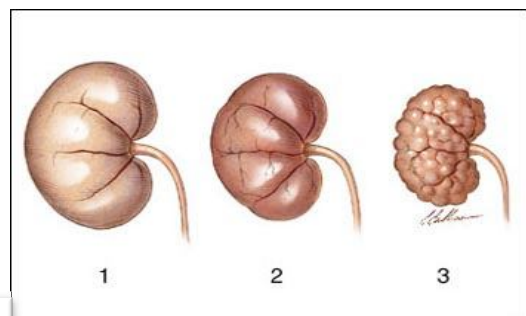
1- Infection	- Chronic pyelonephritis. - Bilateral renal tuberculosis	- Infective endocarditis.
2- Immune	- Chronic glomerulonephritis (end-stage of severe types of GN) - SLE, PAN & anaphylactoid purpura. - Sclerodema.	- Goodpasture's syndrome.
3- Metabolic	- Diabetic nephropathy - Amyloidosis.	- Gouty nephropathy. - Nephrocalcinosis.
4- Malignant	- Multiple myeloma - Wilm's tumour.	- Leukaemia, lymphoma
5- Toxic	- Analgesic nephropathy. - Irradiation.	- Heavy metals e.g. lead, mercury.
6- Vascular	- HTN especially malignant. - Bilateral renal vein thrombosis.	- Recurrent renal infarctions. - Sick cell anaemia.
7- Hereditary	- Polycystic kidney disease. - Renal hypoplasia. - Hereditary nephritis e.g. Alport's syndrome.	- Medullary cystic disease.
8- Obstructive	- Bilateral hydronephrosis	

Pathology:

In Early Stages : There are pathological features of the underlying renal disease.

In Late stages : There are usually features of " end-stage kidney disease":

- Macroscopically: Kidneys are **small** with irregular surface and adherent capsule
except:- PCK - obstructive uropathy - Diabetic nephropathy - Amyloidosis (normal size)
- Microscopically: Diffuse glomerular & tubular atrophy and interstitial fibrosis.



Individuals with chronic kidney failure may remain asymptomatic, even when the functional capacity of kidneys reduces to 20% of the normal capacity. Hence it is recognized as a **'Silent Disease'**.

- 1) H₂O, Electrolyte & A-B
- 2) Cardiovascular
- 3) Respiratory
- 4) Gastrointestinal
- 5) Renal
- 6) Neurological
- 7) Musculoskeletal
- 8) Skin
- 9) Haematological
- 10) Genital
- 11) Metabolic
- 12) Complications of TTT

Clinical manifestations & Pathophysiology:

The clinical manifestations results from both glomerular & tubular dysfunctions.

1) Water, Electrolyte & Acid-base disorders

a. Water balance :

Polyuria: (3-4 L/day)	- unresponsiveness of tubules to ADH. - reduction of medullary hypertonicity. - increased solute load per nephron (osmotic diuresis)
Isothenuria low fixed specific gravity " 1010 "	- Reduced ability of urine concentration and dilution- - increased water intake = hypervolaemia. - decreased water intake = hypovolaemia & dehydration
Oliguria	may occur in the terminal stages

b. Sodium : Two types of abnormality may occur

Na retention	- Na loss " salt-losing nephropathy "
- Commonest - Glomerular (inability to excrete Na) - CVP:- hypervolaemia, HTN, oedema, pulmonary congestion.	- Rare - Tubulo-interstitial diseases - inability of tubules to reabsorb Na - CVP:- hypotension & muscle cramps

c. Potassium:

Total body K is decreased	- loss of intracellular K (acidosis) - decreased intake of K due to anorexia. - use of diuretics.
Serum K is usually increased	extracellular shift

CVP:- manifestations of hyperkalaemia may occur (See later)

d. Metabolic acidosis.

e. Hypocalcaemia, Hyperphosphataemia & 2ry hyperparathyroidism

f. Magnesium & aluminum may be elevated.

2) Cardiovascular Manifestations :

HTN	salt & water retention increased renin decreased renal prostaglandins	CVP:- HF - hypertensive encephalopathy
Atherosclerosis	hyperlipidaemia & hypertension	CVP:- IHDs
Pericarditis	ESRDs (grave)	dry or haemorrhagic painful or painless
Hypotension	salt-losing nephropathy	CVP:- Postural hypotension

3) Respiratory Manifestations:-

1. **Kussmaul's** breathing (rapid deep respiration) due to **acidosis**.
2. **Pulmonary oedema**: due to LVF & increased permeability of alveolar capillaries.
3. Uraemic **asthma**.
4. Recurrent pulmonary **infections** : due to impaired immunity.
5. **Pleurisy**.
6. Ulcers in the respiratory tract:- **hemoptysis**

4) Gastrointestinal Manifestations :

Mouth	a- Uriniferous or ammoniacal odour (uraemic fetor) + bad taste sensation. b- Tongue is dry and coated. c- Stomatitis.
Stomach	a- Anorexia, nausea & vomiting. b- GIT bleeding due to ulceration (PU) & bleeding tendency.
Intestine	6. Constipation. 7. Uraemic dysentery.

+ Increased incidence of **HCV** in patients on regular hemodialysis

5) Renal Manifestations :

1. Polyuria & nocturia. Oliguria may occur in the terminal stages.
2. Urine is pale and watery.
3. Features of the underlying renal disease.

6) Neurological Manifestations : A-P-C-D

- 1) **Apathy**
- 2) **Asterixis**
- 3) **Psychiatric symptoms**: irritability, depression
- 4) **Peripheral neuropathy & myopathy**
- 5) **Convulsions**
- 6) **Confusion & coma**: uremic coma or uremic encephalopathy
- 7) **Dialysis dementia**: usually due to aluminium intoxication
- 8) **Drowsiness, fatigue, headache & lack concentration**

7) Musculoskeletal Manifestations :**I. Renal osteodystrophy** : due to

bone pains & pathological fractures $\pm$ Metastatic calcification (e.g. BV, articular cartilage)	- osteitis fibrosa (2ry hyper-PTh). - osteomalacia. - osteoporosis. - osteosclerosis.
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2. Myopathy.

3. Muscle cramps : may occur due to hyponatraemia.

4. Gout : is rare in spite of hype-uricaemia ??.

8) Skin Manifestations :

1. Pallor & earthy colour of the skin.
2. Pigmentation.
3. Pruritus.
4. Uraemic frost
5. Ecchymosis.
6. Features of dehydration may be present.

**9) Haematological Manifestations :**

Anaemia	- decreased erythropoietin (the most important factor). - deficiency of:- Fe - folate - Haemolysis - BM fibrosis (2ry hyperPTH). - increased aluminum (dialysis)
Bleeding tendency	- abnormal platelet functions (most important). - <i>may be mild decrease of coagulation factors</i>
Increased susceptibility to infections	- decreased lymphocyte functions. - decreased phagocyte functions. - increased exposure to bacteria & viruses (dialysis).

10) Genital Manifestations:

1. **In males** : impotence, gynaecomastia & infertility.
2. **In females** : amenorrhea & infertility.

11) Metabolic Manifestations:

CHD	- Impaired glucose tolerance (uncommonly DM = insulin resistance)
Two types	- Hypoglycaemia = decreased renal clearance of insulin
Lipid	Hyperlipidaemia (increased Tg + decreased HDL) predisposing to atherosclerosis.
Protein	Catabolism leading to wasting & stunted growth in children
Hypothermia	

12) Manifestations due Complications of Therapy:

e.g. complications of dialysis (See later)

Uraemic toxins: products of protein metabolism. role of these substances is unclear.

1. Creatinine, guanidines, indoles, phenols & "Middle Molecules" : may cause

- pericarditis.
- bleeding tendency, haemolysis.
- peripheral neuropathy.
- abnormal carbohydrate metabolism.

2. Urea : may cause:

- ammoniacal breath.
- uraemic frost, pruritus.
- GIT ulceration
- anorexia, nausea & vomiting

Investigations :**1. Urine analysis :**

- Volume: **polyuria** (3-4 L/day). *Oliguria may occur in the terminal stages.*
- Aspect : pale & watery.
- Specific Gravity : **low fixed** " 1010 "
- **Proteins** : more marked in glomerular disorders.
- Microscopic examination : granular & **broad casts**.

2. Blood investigations :

- Normochromic normocytic anaemia.
- Serum Na may be increased or decreased.
- Serum K is usually **increased** (*ECG more sensitive for K disturbances*)
- Decreased Ca & increased P. - Decreased HCO₃, pH.

3. Renal function tests : There is marked impairment of renal functions :

- Increased blood urea, serum creatinine & uric acid levels.
- Decreased creatinine clearance (a good estimate of GFR).

4. Renal imaging:

- Plain X-ray of urinary tract (**PUT**). - Ultrasonography.
- IVP (only if blood urea < 100 mg %) & ascending, pyelography.
- CT & MRI.

5. Renal biopsy : Shows features of the pathology (See before,)**6. Investigations for the cause.****7. Investigations for detection of complications:** e.g.

- Plasma lipids.
- Radiologic examination of bones.

Treatment:

TTT of chronic kidney diseases:-		
	GFR	TTT
1	≥ 90	1- Diet
2	60 – 89	2- Symptomatic
3	30 – 59	3- ttt of the cause
4	15 – 29	±
5	< 15	ESRD:-Dialysis-transplantation

1. Diet:

Fluids	Fluid intake depends on urine output & other losses . Usually 3 L/day are given to maintain fluid balance of the body.
Salt	- In cases of HTN, HF: salt intake should be restricted. - In case of hypotension (<i>salt-losing</i>): salt intake should be increased.
K	Restricted in advanced cases & if there is hyperkalaemia
Proteins	- Restricted to 0.5-1 gm/kg/day (slow the progression of the disease). - Proteins rich in essential amino acids should be used.
CH	Adequate amounts of carbohydrates are given to ensure sufficient caloric intake & limit protein catabolism
Fats	Better to be restricted since uraemic patients may have hyperlipidaemia.

II- Symptomatic Treatment : e.g

Acidosis	- Sodium bicarbonate : 1-3 gm/d orally.
HTN	Slow and gradual (to avoid renal hypoperfusion) - Salt restriction. - Anti-hypertensive drugs: - Diuretics e.g. frusemide or thiazides. - B-blockers. - Ca-blockers. - Methyldopa. - Hydralazine - ACE-I could be used especially in DM unless (hyperkalaemia - Creatinine > 3 mg%)
Anaemia	- Erythropoietin - Fe & folate - Packed red cell transfusions.
Osteodystrophy	- Reduction of phosphate : diet - Ca carbonate or aluminum HO - Calcium supplementation: 1-2 gm/day. - Vitamin D : e.g. 1,25 dihydroxyvitamin D3.
Others	HF:- see CVS (Digitoxin) Hiccough:- chlorpromazine & anti-histaminics

In all drugs:- avoid nephrotoxic & adjust the dose (based on GFR) as:-

GFR > 50	GFR = 50 - 10	GFR < 10 (if on dialysis)
Full doses - May be 75% in some drugs	50-75%	Usual if on dialysis

III) Treatment of the Cause: e.g. adequate control of DM

TTT of Aggravating factors: e.g UTI - Avoidance of nephrotoxins

IV) Treatment of End-Stage Renal Failure :**A-Dialysis** : "Regular Dialysis Treatment"**- Indications:-**

Clinical:- Conservative treatment becomes inadequate

Lab:- Creatinine > 10 mg % or creatinine clearance <10 ml/min

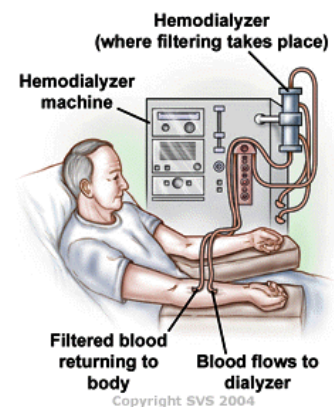
- Methods :

- Haemodialysis : 2-3 times weekly.

- Peritoneal dialysis : rarely used for chronic dialysis

- Complications

Haemodialysis	- Peritoneal dialysis
- Infections. - Hepatitis.	- Osteodystrophy - Amyloidosis.
- Hypotension - Air embolism	- Peritonitis. - Hernias. - Hyperglycaemia.
- N&V. - Dialysis dementia.	- Dialysis disequilibrium syndrome

**B. Renal Transplantation :**

- This is the only curative treatment for irreversible renal failure.

- HLA-matching. - Immunosuppressive to prevent rejection

- **Complications**:- 1-Non-function of the graft. 2- Rejection of the graft.

3- Opportunistic infections. 4- Malignancies. 5- Hypertension.

6- Recurrence of the original disease.

ACUTE PYELONEPHRITIS

Definition:- inflammation of the kidney parenchyma, calyces and pelvis.

"pyelitis" means inflammation of the pelvis and calyces

Aetiology:

A) Causative Organisms:

- **Gram-negative bacilli :** (90 % of cases)
 - E. coli (about 80 % of cases).
 - Proteus, Klebsiella, Pseudomonas, Enterobacter.
- **Gram-positive cocci:-** Staph. aureus & saprophyticus, Strept. faecalis
- **Other organisms :** fungi, chlamydia, viruses.

B) Routes of Infection :

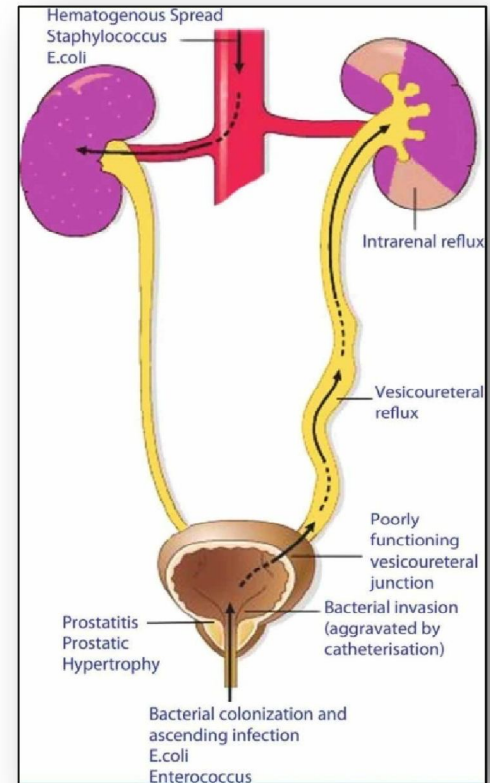
1. Ascending infection : (the most common)
From lower urinary tract either **transluminal** or through **periureteric** lymphatics.
2. Haematogenous route: (uncommon) bacteraemia
e.g. SBE, pneumonia
3. Lymphatic route.

C) Predisposing Factors :

1. Stagnation of urine: Due to obstruction at any level of urinary tract due to stones; strictures, tumours, enlarged prostate, neurogenic bladder.
2. Vesico-ureteric reflux.
3. Impaired immunity : e.g. Diabetes mellitus. - Extremes of age. - Immunodeficiency diseases
4. Introduction of Infection:
 - Catheterization, cystoscopy, bladder surgery.
 - Honeymoon cystitis. ,
5. Pregnancy: decreased ureteric peristalsis & temporary incompetence of vesico-ureteric valves.

Pathology:

- The condition may be unilateral or bilateral.
- There is inflammation of mucous membrane of the pelvis
- Infection mainly involves the renal medulla.
- Multiple micro-abscesses may be seen in the kidney.



Clinical Picture:

Symptoms:

- General symptoms : Acute onset of fever with rigors, headache & malaise.
- Abdominal symptoms :
 - Acute pain in the loin radiating to the groin.
 - Frequency, urgency, dysuria, pyuria & strangury may occur
 - Nausea, vomiting & may be diarrhea.

Signs:

- General signs : Fever, tachycardia, pallor & sweating.
- Abdominal signs :
Tenderness & rigidity over the affected kidney (in the costovertebral angle & on deep abdominal palpation).

- Complications :**
- Septicaemia.
 - Pyonephrosis.
 - Recurrence of infection & progression to chronic pyelonephritis
 - Perinephric abscess.
 - Acute renal failure (rare).

Acute Necrotizing Papillitis:

- Usually occurs in diabetes, urinary tract obstruction & sickle cell anaemia.
- There is severe infection leading to papillary necrosis.
- The patient presents with:
 - Severe pyelonephritis.
 - severe haematuria & necroturia.
 - urinary tract obstruction.
 - acute renal failure (ARF)

Investigations:

1. Urine analysis :

- Volume:- normal & rarely oliguria in cases complicated by ARF.
- Aspect:- **turbid** or normal.
- pH:- **acidic** in most cases (E, coli) & **alkaline** with urea-splitting bacteria (**proteus**)
- Proteins: mild proteinuria.
- Microscopic examination :
 - Cells : - Many **pus** cells
 - Epithelial cells.
 - Casts : **White cell casts**, epithelial casts & hyaline casts.
 - Some RBCs.
 - + Bacteriuria.**

2. Urine culture & sensitivity test:

Quantitation of number of bacteria is important to differentiate infection from contamination:

- bacterial count more than 100,000/ml denotes infection.

- bacterial count less than 10,000/ml denotes contamination

3. **Blood picture** : Polymorphnuclear leucocytosis

4. **Renal function tests** : Normal except rarely in cases complicated by ARF

5. **Renal imaging** :

e.g. X-ray & ultrasonography are required for detection of predisposing factors (e.g. stones) & complications (e.g. perinephric abscess).

Other investigations such as IVP & cystoscopy may be needed for detection of predisposing factors especially in recurrent pyelonephritis, but better to be avoided during acute severe diseases.

Differential Diagnosis :

Acute pyelonephritis should be differentiated from other conditions presenting with:

1. Fever with rigors:
2. Abdominal pain.
3. Pyuria e.g. cystitis:

Treatment:- 4 (as any infection)

1) General care :

- Rest in bed.
- Light nutrient diet.
- Excessive fluid intake

2- Symptomatic:- eg. antipyretic for fever

3) Specific treatment :

A. Antimicrobial drugs : - Before C\S, a broad spectrum antibiotic is given e.g.

- Tetracyclines e.g. doxycycline 100 mg/12 h orally.
- Amoxicillin 500 mg/8 h orally.
- Co-trimoxazole 2 tab/12 h orally.
- Quinolones e.g. ofloxacin 200 mg/12 h orally.

- Resistant & recurrent cases are treated according to culture & sensitivity e.g.

E. Coli	- Tetracyclines, amoxicillin, co-trimoxazole - quinolones. - Nitrofurantoin - Nalidixic acid.
Pseudomonas	Carbimicillin or piperacillin
Gm-ve bacilli	Gentamycin : 80 mg/8 h IV or IM. or - Amikacin : 7.5 mg/kg/12 h IV

- Duration of therapy is usually 7-14 days.

B. Change the urine pH :

- If urine is acidic : NaHCO₃ or K citrate 2 gm t.d.s
- If urine is alkaline : Ascorbic acid 1 gm/d.

C. Urinary antiseptics: e.g. M mandelate:- prophylaxis against recurrent infections.

4) Treatment of complications and Correction of predisposing factors:

e.g. calculi,, obstruction.

CHRONIC PYELONEPHRITIS

Definition:- continuing pyogenic infection of the kidney, can result in scarring of the renal parenchyma and impaired function.

Aetiology: It usually occurs in patients with underlying abnormalities e.g. urinary tract obstruction, vesico-ureteric reflux & impaired immunity.

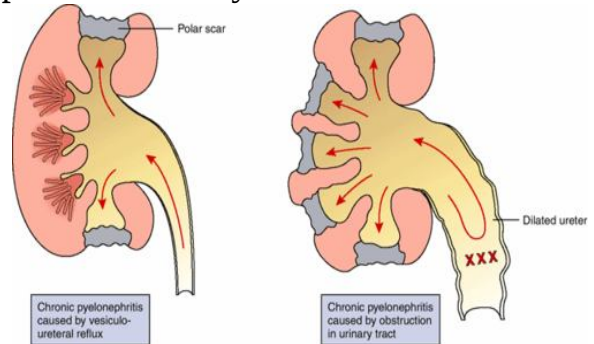
Pathology:

Macroscopic appearance:-

- The disease may be unilateral or bilateral. If bilateral, it is usually asymmetrical.
- The affected kidney is **small** with **irregular** surface & **adherent** capsule.

Microscopic appearance :

- The process is **patchy** & affecting mainly the interstitium of the medulla & papillae.
- There is chronic **inflammatory** cells & **fibrosis** in the interstitial tissue.
 - The tubules are **atrophic** & **dilated**.
 - In glomeruli early normal, then show **fibrosis** & **hyalinosis**.



Clinical Picture:-

The patient may present with one or more of the following manifestations :

1. **Recurrent** attacks of loin pains, frequency, dysuria, pyuria & fever
2. **Non-specific** symptoms e.g. fatigue, back pain, abdominal discomfort, anorexia & loss of weight.
3. Progression to **chronic renal failure**.
4. **Hypertension**.
5. **Anaemia**.
6. Tubular dysfunction e.g. salt-losing **nephropathy**, **proteinuria**.

Investigations:

1. Urine analysis :

- **Proteins** : usually less than 2 gm/24 h.
- **Pus** cells & **white** cell casts : may be present.
- In late stages : features are similar to cases of **CRF (write)**

2. Urine culture & sensitivity

3. Blood picture : - Anaemia.

- $\pm$ leucocytosis.
- Increased ESR.

4. Renal function tests :

- In late stages : similar to cases of **CRF (write)**.

- Tubular functions are impaired more than glomerular functions
- Differential renal function tests: usually show a difference between the function of both kidneys.

5. Renal imaging : (X-ray, IVP & ultrasonography).

- Show small-sized kidneys (usually unequal) with calyceal deformities
- May detect predisposing factors e.g. stones, strictures.

6- Renal biopsy : (See pathology)

Treatment:

1. Correction of the **predisposing** factors.
2. **Antibiotic** therapy:
 - Selection of antibiotics is based on culture & sensitivity tests.
 - Antibiotics are used in reduced doses because of impaired function.
 - Prolonged & repeated courses of treatment may be needed.
3. Treatment of **CRF & HTN** if present.
4. Unilateral nephrectomy (rarely) in advanced unilateral cases with complete loss of function.

Renal Tuberculosis

Aetiology:

- Causative organism : *Mycobacterium tuberculosis*.
- Mode of infection:- Usually due to **haematogenous** spread from a primary lesion.
- May occur in **immunocompromised** patients e.g. AIDS.

Clinical Picture :

Symptoms :

1. General symptoms : Night sweat, night fever, anorexia, loss of weight & fatigue.
3. Abdominal symptoms:-
 - Loin pain.
 - Frequency, dysuria, pyuria & haematuria.

Signs:

1. General signs : Loss of weight, pallor, toxic facies & fever
2. Abdominal signs : May be tenderness over the affected kidney

Features of active T.B. may be detected (e.g. lung TB)

Complications:

1. Ureteric **strictures** and **Obstructive** uropathy.
2. Bilateral cases may end in **CRF**
3. **Spread** e.g. genital tuberculosis.
4. Secondary **amyloidosis**.

Investigations:**1) Laboratory investigations :**

- 1- ESR : markedly elevated.
- 2- C-reactive protein : elevated.
- 3- Blood picture : normochromic normocytic anaemia.

2) Urine analysis :

- Sterile pyuria (pus in urine with no bacterial growth)
- Haematuria.
- Urine is subjected to :
 1. Smear stained with Ziehl-Neelsen stain.
 2. Culture & sensitivity test using Lowenstein-Jensen medium or BAC-TEC
 3. Animal inoculation in guinea pig

3) Abdominal ultrasonography or IVP: may show

- Hydroureter & hydronephrosis.
- Ureteric strictures.
- Calcification.

4) Renal biopsy:-

Show characteristic granulomatous lesions consisting of a central area of caseation surrounded by lymphocytes, epithelioid cells, Langhan's giant cells & fibroblasts. T.B. bacilli may be detected.

5) New Investigations :

- Detection of mycobacterial DNA by PCR.
- Detection of serum IgG against mycobacterial antigens by ELISA.

6) Tuberculin test : usually positive.**7) Chest X-ray : May show pulmonary T.B.****8) Therapeutic test : using antituberculous drugs.****Treatment:**

- 1) General care :
 1. Rest in bed.
 2. Proper nutrition.
- 2) Symptomatic treatment : e.g. antipyretics for fever.
- 3) Specific treatment : (Refer to Chest Diseases).
- 4) Surgery : may be required e.g. for ureteric obstruction.

- Amyloidosis.
- Drugs e.g. outdated tetracyclines.
- Heavy metals e.g. mercury, lead.
- Nephrotic syndrome.

Manifestations:

- | | |
|--|----------------------------|
| 1. Renal glycosuria. | 2. Aminoaciduria. |
| 3. Phosphaturia (rickets or osteomalacia). | 4. Renal tubular acidosis. |
| 5. Hypokalaemia. | 6. Polyuria. |

Treatment:

- Fluid and electrolyte replacement ~ HCO_3 , Na, K & phosphates.
- Vitamin D.
- Treatment of the cause if possible.

RENAL TUBULAR ACIDOSIS **(R TA)**

Definition:- It is medical condition that involves an accumulation of acid in the body due to: Failure of the kidneys to appropriately acidify the urine

Aetiology:

1. **Genetic** :
 - Isolated.
 - Wilson's disease.
2. **Acquired** :
 - Drugs e.g. analgesic nephropathy, amphotericin B
 - Nephrocalcinosis.
 - Sjogren's syndrome.

Manifestations :

1. Metabolic acidosis with alkaline urine.
2. Rickets or osteomalacia.
3. Nephrocalcinosis & renal calculi.
4. Hypokalaemia.
5. Polyuria.

Treatment:

- Fluid and electrolyte replacement : HCO_3 & K
- Vitamin D.
- Treatment of the cause if possible.

PROTEINURIA

Definition: Presence of more than 300 mg of proteins in 24-hour urine.

Aetiology:

Glomerular	> 2-3 gm/day	causes of <i>nephrotic & nephritic syndromes</i>
Tubular	<2 gm/day	causes of <i>interstitial nephritis</i>
Overflow	0.2 - 10 gm/day	Filtration of low molecular weight proteins. 1. Bence-Jones proteinuria in multiple myeloma. 2. Haemoglobinuria in intravascular haemolysis. 3. Myoglobinuria in rhabdomyolysis.
Miscellaneous	<2 gm/day	1. Orthostatic proteinuria. 2. Heart failure. 3. Fever. 4. Anaemia 5. Heavy exercise. 6. Convulsions.

False proteinuria:- results from loss of protein from the lining of the urinary tract
e.g. in infections & haematuria

Micro-albuminuria:

- It is the excretion of small amounts of albumin in urine (30-300 mg/day)
- It is an early indicator of *diabetic nephropathy*
- measured by *radioimmunoassay*.



Polyuria

Definition:- Volume of urine > 1500 cc/day (depends on fluid intake)

Causes:-

Physiological	- Excessive water drinking - Excessive tea, coal, coffee	- Exposure to cold
Renal	- Polyuric phase of ARF - Early stages of CRF - Nephrogenic DI	- Diuretics - Following renal transplantation
Endocrinal	- Diabetes insipidus DI - Thyrotoxicosis - Hyperparathyroidism	- DM - Cushing - Conn's syndrome
Others	- Reidel's crisis - Migraine	- Supraventricular tachycardia

Hematuria

Definition - Presence of blood more than 5 RBCs / HPF in urine

Causes:

Pre-renal	Hemorrhagic blood diseases e.g hemophilia, DIC or anticoagulants
Renal	<u>Renal injury</u> :- trauma, renal stones <u>Renal inflammation</u> : pyelonephritis <u>Renal tumors</u> : hypernephroma <u>Vascular</u> :- renal infarction or malignant HTN, renal vein or IVC thrombosis
Post-renal	<u>Ureter</u> : stone, trauma <u>Bladder</u> : tumor, cystitis, stone Prostate: tumor, or enlargement <u>Urethra</u> : stone, tumor, urethritis

Diagnosis of a case hematuria

Clinically:- (stress on timing of haematuria)

In pre-renal causes: Bleeding from other body sites

In renal causes: hematuria is the same throughout voiding

There is evidence of renal disorder (e.g. renal colic)

The kidney examination:- o Enlarged: in tumors or hydronephrosis
o Tender renal angle in pyelonephritis

In post-renal causes:

There is initial hematuria in prostatic and urethral causes

There is terminal hematuria in bladder causes

Investigations

1. Coagulation profile, bleeding time, and platelet count
2. Laboratory investigations for the cause: e.g. ANA, rheumatoid factor
3. Urine analysis: for casts, proteinuria, crystaluria
4. Renal imaging: sonography, CT, radio-isotopic studies, Doppler for renal arteries and veins
5. Cystoscopy

Differential diagnosis:

Red urine	Dark urine
1. Drugs: rifampicin	1. Drugs: ambilhar, adriamycin, phentoin, chlorequine
2. Hemoglobinuria: causes of hemolytic anemia, e.g PNH	2. Dies: phenolphthalein
3. Myoglobinuria: crush syndrome	3. Diet: colouring material in sweets
	4. Diseases: obstructive jaundice, porphyria

Drugs & kidney

Drugs induced impairment of renal functions

a) Pre renal: hemodynamic kidney injury (hypo-perfusion)

- ACEIs: via VD reducing inter-glomerular pressure particularly in RAS.
- NSAIDs: inhibition of vasodilatory prostaglandin synthesis

b) Renal

1- Acute tubular necrosis (nephrotoxins)

- Antibiotics: Aminoglycosides (gentamicin, streptomycin), Amphotericin B
- Heavy metals: Arsenic, Mercury
- Radiographic contrast media

2- Glomerulonephritis

Minimal change GN:- NSAIDs - Ampicillin - Interferon -

Membranous GN:- Gold - Penicillamine

Focal segment GN:- Heroin

Proliferative GN:- Allopurinol - Penicillin - Sulfonamide - Amphetamine IV

Rapidly progressive GN:- Amoxicillin - Penicillamine - Carbimazole - Warfarin

3- Acute tubulointerstitial nephritis

Hypersensitivity reaction to drugs:- NSAIDs - Penicillin - Sulphonamides

4- Chronic tubulointerstitial nephritis:- NSAIDs (analgesic nephropathy)
Nephrogenic DI: Lithium

c) Post renal Urinary tract obstruction:

- Crystal formation: Acyclovir
- Hemotherapy: uric acid crystals forming as a consequence of tumor lysis
- Retro-peritoneal fibrosis: Methysergide

Drug eliminated mainly by the kidneys:

May accumulate in patients with low GFR leading to toxic effect e.g

- o Digoxin: arrhythmias
- o Erythromycin: encephalopathy
- o Lithium: arrhythmias, seizures
- o Penicillins & cephalosporins: encephalopathy

Electrolytes imbalance		
	Hypernatremia	Hyponatremia
Causes	1. ↓ H ₂ O intake: old age 2. Hypotonic fluid loss: 3d - Diarrhea, vomiting, sweating - DI - DM 3. Na retention:- (C) CRF, Conn's, Cushing & Cirrhosis 4. Hypertonic fluid gain	1. ↑ H ₂ O intake: hysterical polydipsia 2. Over-hydration=water intoxication* See Below 3. Na loss: - Renal: Addison, diuretics - GIT: vomiting diarrhea 4. Excessive hypotonic saline
C/P	1. <u>Features of the cause</u> : CRF 2. <u>General</u> : polydipsia, nausea, vomiting & Muscle twitches ... 3. <u>Neurological</u> :- Confusion, Convulsions, loss of Concentration, coma, Irritability 4. <u>Depends on EVC (Extra-Cellular Volume)</u> it may be - Hypervolemic hyperNa:- C/P of hypervolemia ---- Hypovolemic hyperNa:- C/P of hypovolemia (ABP)	
TTT	• ↓ Na intake • Hypotonic fluid infusion • Hypotonic saline + lasix in hypervolemic hypernatremia • TTT of the cause NB: slow correction to prevent brain edema	• ↑ Na intake • Hypertonic saline + lasix in a case of hypervolemia • Treatment of the cause

Hypervolaemia with Dilutional Hyponatraemia (Overhydration - Water intoxication)

<u>Aetiology</u>	<u>C/P As Hyponatremia</u>	<u>TTT:- As Hyponatremia</u>
1. ARF if excessive fluids are given. 2. Post-operative & post-traumatic states. 3. Syndrome of inappropriate secretion of ADH (SIADH): - Paramalignant e.g. bronchogenic carcinoma, lymphoma - CNS lesions e.g. tumour, trauma, infection. - Chest diseases e.g. tumour, pneumonia, T.B. 5. Oedematous conditions (e.g. CHF, constrictive pericarditis, LCF) especially with diuretic therapy.	+ Main:- (CNS) - Dizziness, weakness, headache & vomiting. - Confusion, muscle twitches, convulsions, coma & finally death.	Main:- <u>Fluid restriction.</u>

	Hyperkalemia	Hypokalemia
Causes	<u>Increased intake:</u> "iatrogenic" - Excessive therapy with IV potassium - Excessive transfusion of stored blood <u>Decreased loss</u> - Renal failure: acute & Chronic - Adrenal failure: Addison's disease - Drugs:- K-sparing diuretic - ACE inhibitor <u>Extracellular shift</u> - Acidosis - Insulin deficiency - Tissue lysis: hemolysis, rhabdomyolysis, tumour	<u>Decreased intake</u> - IV fluid therapy deficient in potassium - Diet: deficient in potassium - Decreased absorption: malabsorption syndrome <u>Increased loss</u> - Renal loss: Non potassium-sparing diuretics - Adrenal:- Cushing's S. & Conn's S. & steroid ttt. - GIT loss:- Diarrhea (secretory) - Vomiting - Excessive tapping of ascites <u>Intracellular shift</u> - Alkalosis -Insulin therapy - Diet rich in CHO
C/P	<u>Heart:</u> Bradycardia, HB, Cardiac arrest in diastole <u>Muscle:</u> Myopathy, Weakness, Paralysis	<u>Heart:</u> Arrhythmias (in patients receiving digitalis) <u>Muscle:</u> Myopathy, Weakness, Paralysis <u>GIT:</u> Constipation, distension, paralytic ileus <u>Kidney:-</u> Damage of the renal tubules <u>CNS:</u> Tetany due to associated alkalosis
Lab.	<u>Serum K:</u> Increased (normal: 3.5 – 5 mEq/L) <u>ECG:</u> P-R interval: prolonged - QRS: widened T wave: tall & peaked ± Bradycardia, HB <u>Investigations for the cause:-</u> e.g. KFTs	<u>Serum K:</u> Decreased (normal: 3.5 – 5 mEq/L) <u>ECG:</u> ST segment: depressed T wave: flat or inverted Prominent U wave <u>Investigations for the cause:-</u> e.g. malabsorption

TTT	<u>Decreased intake</u> Diet: restriction of potassium in diet Drugs: restriction of spironolactone & captopril Decrease absorption:- cation-exchange resins <u>Increased loss:- Diuretics (frusemide)</u> - Dialysis if K > 7 <u>Intracellular shift</u> - Correction of acidosis: NaHCO ₃ 100 mEq IV - Insulin + glucose:	<u>Potassium replacement:</u> in severe cases: IV potassium with careful monitoring in mild cases: oral potassium is preferred to avoid hyperkalemia <u>Treatment of the cause</u>
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Antagonize the effect of hyperkalemia on heart Calcium gluconate: 10 ml of 10% solution over 10 minutes

ACID-BASE BALANCE

$$- \text{pH} = \text{pK}' + \log \frac{\text{HCO}_3^-}{\text{HCO}_3}$$

- Normal pH = 7.35 - 7.45

	Metabolic acidosis	Respiratory acidosis
Causes	<u>Increased acid:</u> a) increased acid production: • Endogenous: diabetic ketoacidosis, Lactic acidosis • Exogenous: Salicylates, Methyl alcohol b) Decreased acid excretion: • Renal failure: Acute & Chronic <u>Decreased alkali:</u> a) GIT causes: • Severe diarrhea • Fistula: pancreatic, biliary, intestinal b) Renal causes: • Tubular defects: Fanconi syndrome, Renal tubular acidosis • Drugs: Spironolactone	- All causes of hypercapnic respiratory failure that occur due to hypoventilation: "Refer to chest"

CVP	1. <i>Respiratory</i> : Hyperventilation: Kussmaul's breathing 2. <i>Heart</i> : Myocardial depression 3. <i>Bone</i> : Decalcification in chronic cases 4. <i>CNC</i> : Drowsiness $\pm$ impaired consciousness	- Features of respiratory failure: "refer to chest"
TTT	1. NaHCO ₃ IV 2. Treatment of the cause	- Treatment of respiratory failure: "Refer to chest"

	Metabolic alkalosis	Respiratory alkalosis
Causes	1. <u>Increased intake of alkali</u> : - Excessive ttt with bicarbonate - Milk-alkali syndrome in ttt of P.U. 2. <u>Decreased acid</u> - GIT loss: vomiting & gastric drainage - Renal loss: Diuretics, Conn's S, Cushing S 3. <u>Hypokalemia</u>	<u>All causes of Hyperventilation: e.g.</u> - Hysteria - Head injury or encephalitis - Heat stroke - Heart failure or pulmonary embolism or pneumonia
CVP	1. Respiratory: Hypoventilation: shallow slow 2. Tetany 3. Manifestations of hypokalemia may occur	1. Hyperventilation 2. Parasthesia 3. Tetany: in severe cases
TTT	1. Treatment of the cause 2. Diluted HCL: in severe cases	1. Treatment of the cause 2. Hysterical cases: should re-breathe in a paper bag + sedation

Investigations:-

	Metabolic Acidosis	Respiratory Acidosis		Metabolic alkalosis	Respiratory alkalosis
pH	Low	Low		High	High
HCO₃	Low	High		High	Low
PCO₂	Low	High		High	Low

2- Investigations for the cause